USDA Annual Report 2012
14-R-0031

Explanation of Category E Items

Number of Animals and Species Used:
Infectious Disease Research
Species: 535 Hamsters
Category E: 156

Procedure used:
Disease is induced in hamsters by the administration of clindamycin and a suspension of *Clostridium difficile* bacteria which mediated by secreted toxins. Diarrhea develops 1-5 days after induction and ranges in severity from mild ("wet tail") to acutely fatal as a result of bacterial toxins.

Measures to detect and relieve pain:
All animals are checked at least twice a day seven days a week by research and facility staff. Each animal's health is scored for weight and behavior in addition to disease symptoms (diarrhea). As a result of this monitoring procedure, we are almost always able to humanely euthanize animals at the first sign of significant pain or disease. We report these animals in Category D. Because of the acute effect of the bacterial toxin, a number of animals are found dead without preliminary signs of disease. We report this subset of animals in Category E.

Justification:
Clostridium difficile associated diarrhea (CDAD) is a serious unmet medical need, causing severe to fatal disease in more than 300,000 patients per year, including more than 1% of all hospitalized patients. The hamster model exhibits the same pathophysiology as the human disease and is the gold standard model for CDAD research into prevention and treatment of this condition. The scientific literature has not described any successful treating disease symptoms in hamsters.

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Explanation of Category E Items

Number of animals and species used:
Infectious Disease Research
Species 43 Guinea Pigs
Category E: 5

Procedure used:
This procedure is used as a model for recurring herpes simplex virus-2 disease. The initial infection is induced by the administration of a suspension of herpes simplex virus-2. As a refinement, animals receive an infusion of purified human immunoglobulin to reduce mortality and morbidity during the acute phase of the disease. Acute disease appears within 7-10 days and lasts approximately 14 days.

Measures to detect and relieve pain:
During the acute phase, research staff checks all animals twice a day seven days a week. The scoring system includes an assessment for urine retention, neurologic impairment, the extent and severity of viral lesions and an overall evaluation of activity, appetite and body condition. Animals with moderate virus lesions receive pain medication (buprenorphine 0.05 mg/kg SQ BID or sustained release buprenorphine 1.2 mg/kg SQ q3days) and supportive care. Animals with severe lesions or which do not respond to analgesia are euthanized. We report these in Category D. A small number of animals with rapidly progressive disease are found dead or are euthanized in a moribund condition. We report these in Category E.

Justification:
The focus of this research is to develop a therapeutic vaccine for recurring herpes simplex virus-2 infections. Herpes simplex virus-2 disease affects over 530 million people around the world. A fourth of them suffer painful recurrences during their lifetime for which there is no effective cure. Current therapeutic treatment of the symptoms from recurrent disease is only partially successful and therefore there is a significant unmet medical need for a therapeutic vaccine for herpes simplex virus-2.